HelmholtzZentrum münchen
German Research Center for Environmental Health

Statistical inference for large-scale ordinary differential equation (ODE) models of cancer signaling

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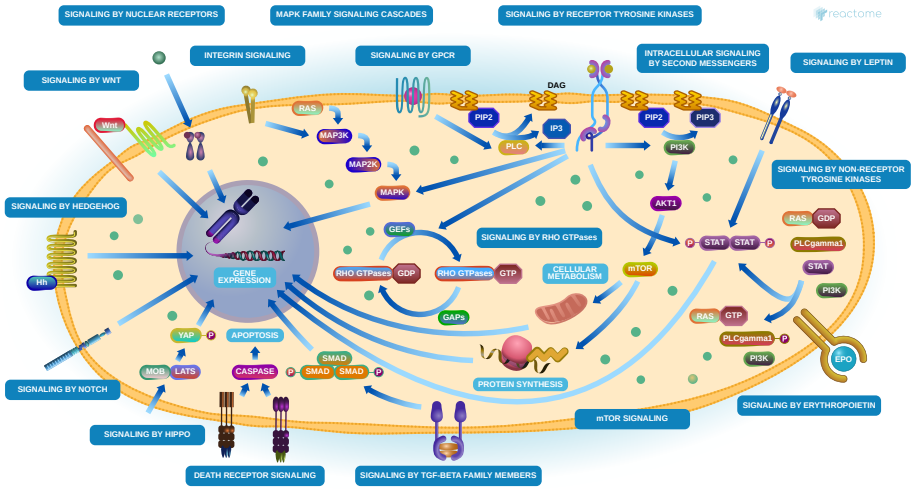
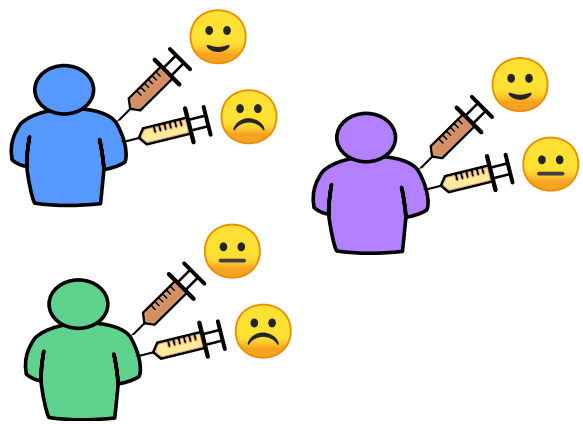
Background

- Complex dynamics in biochemical signaling networks
- Cancer as heterogeneous disease with highly variable treatment outcomes
- Large and complex datasets to be analyzed

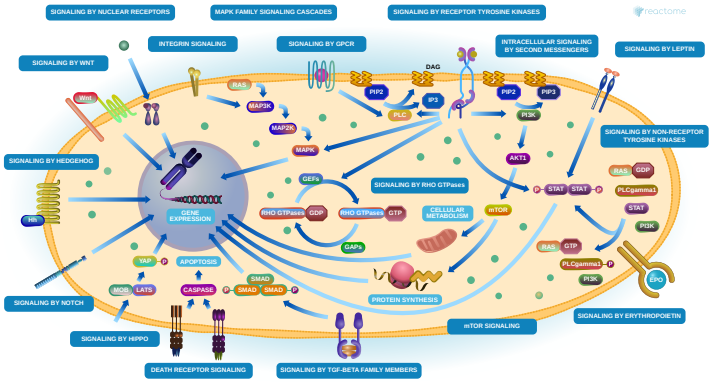
→ **Goal: Model-based prediction of patient responses**



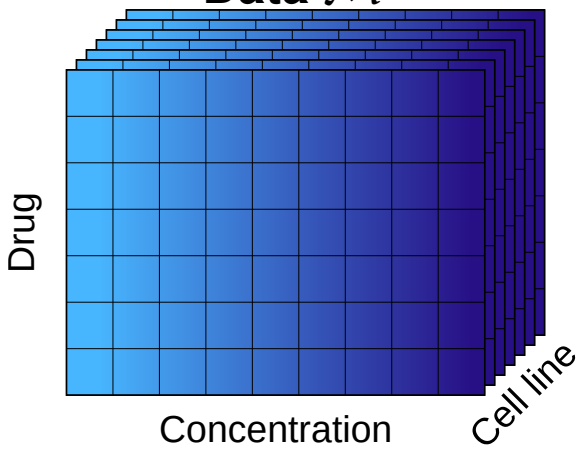


Data integration using ODE models & parameter inference

Model $\mathcal{M}$



Data $\mathcal{M}$



e.g. `ProteinA + ProteinB` $\underset{k_f}{\overset{k_r}{\rightleftharpoons}}$ `ProteinA:ProteinB`

$$\dot{x}(t,\theta,u = f(x(t,\theta,u),\theta,u), \quad x(t_0,\theta,u) = x_0(\theta,u)$$

$\rightarrow$ Gradient-based optimization of likelihood $p(\mathcal{D}|\mathcal{M})$
$\rightarrow$ Objective function evaluation requires
potentially large number of costly model simulations

Scalable simulation and parameter estimation — parPE & AMICI

High performance computing for parameter estimation

- many large systems of ODEs
- non-convex optimization problem

Simulation: **AMICI**[1]

- Scalable simulation and sensitivity analysis using adjoint approach
- CVODES interface
- C++, Python, Matlab interface

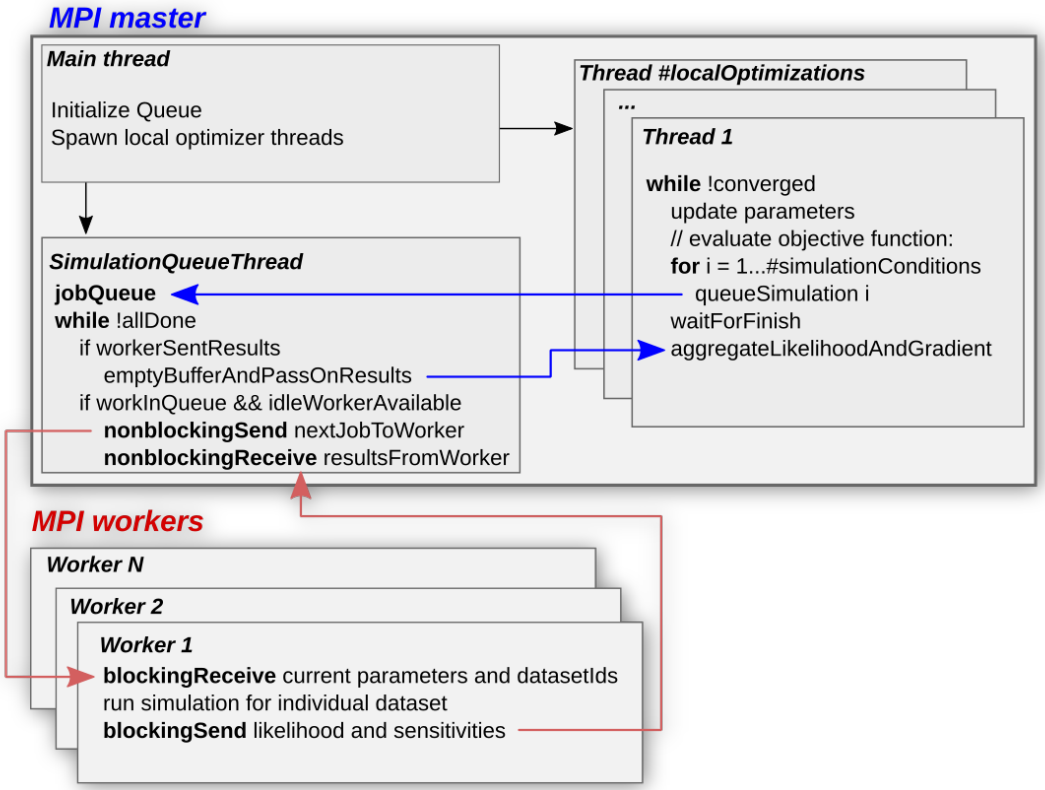
`https://github.com/ICB-DCM/AMICI/`

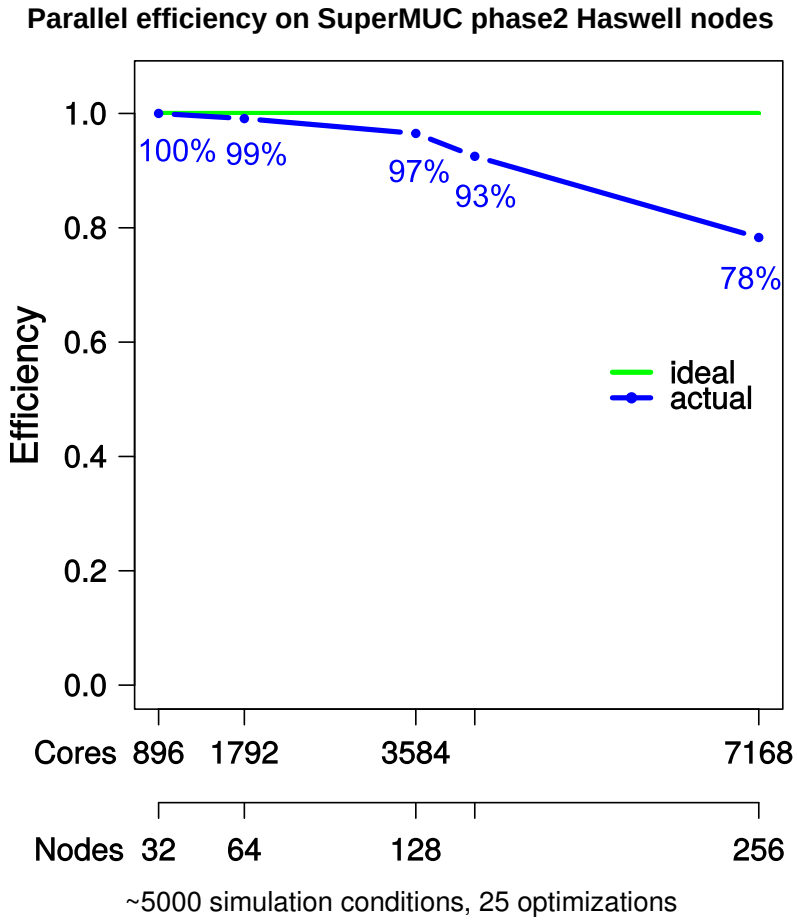
Optimization: **parPE**[2]

- Distributed parallelization of model simulation
- Mini-batch and optimization and interfaces to batch optimizers
- C++ library

`https://github.com/ICB-DCM/parPE/`

Parallelization & scaling



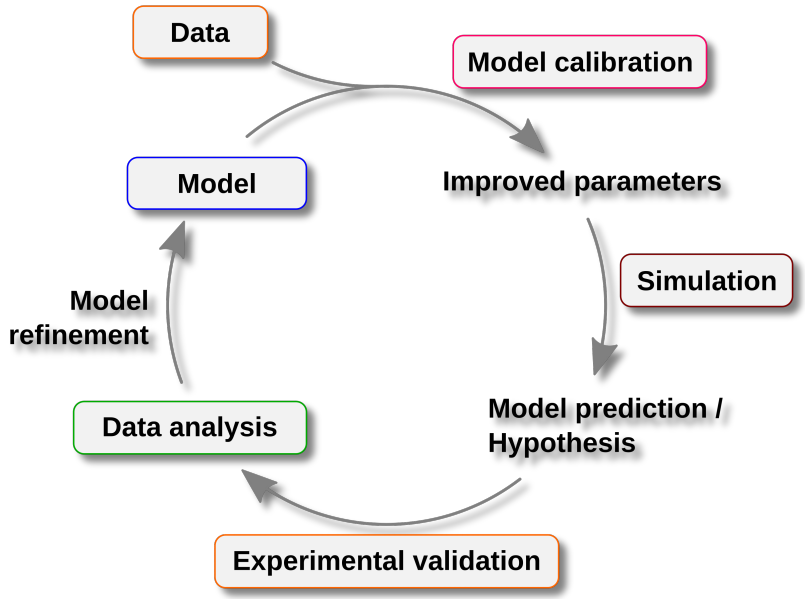


~5000 simulation conditions, 25 optimizations

Application — CanPathPro [3] (http://canpathpro.eu/)

- Deep phenotyping of mice
- Data integration using mechanistic model
- Predictive modelling platform

→ In silico experiments:
optimal treatments, effect of mutations, ...



[3] CanPathPro in 2min: https://player.vimeo.com/video/312066145

Acknowledgements

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